

REMARKS/ARGUMENTS

Reconsideration of this application in view of the foregoing amendments and the following remarks is respectfully requested.

With this amendment, claims 1, 2, 4, and 86 through 89 are in the case. Claims 1, 2 and 4 have been amended. Claims 3, 5-12, and 85 have been cancelled. New claims 86-89 have been inserted.

i. The Rejections under 35 USC § 102(b)

In the action, the Examiner has applied the reference of Che et al. ("*Studies on Synthesis and Catalytic Activity of New Polymer Supported Chelated Titanate*", Hechen Huaxue, Volume 6, No. 1, 1998) against claims 1 and 3 as being unpatentable over Che et al. The Examiner indicates that the Che et al. reference teaches Applicant's claimed polymers, wherein in Che et al., chloromethylpolystyrene is used to react the dihydroxyalkylamine to produce the same structure as is claimed by Applicant. This rejection is overcome.

Applicant has presently incorporated the limitation of claim 3 into claim 1 and has further amended claim 1 to specify that the solid support comprises a polystyrene that is cross-linked and having about 1% to 2% cross-linking. Support for this amendment can be found at page 4, fourth paragraph of the description as filed which discloses solid supports comprising poly(styrene-divinylbenzene) or an equivalent composition that is preferably cross-linked with about 1% to 2% divinyl benzene. Likewise, page 5, fifth paragraph of the description as filed discloses solid supports comprising N,N-diethanolaminomethyl-conjugated polystyrene, with cross-linking preferably about 1% to 2%. Also, page 27, last paragraph through to page 28, first paragraph discloses polystyrene that has a low-degree of divinylbenzene cross-linking, preferably about 1%-2% is preferred to optimize resin swelling and reagent diffusion.

Applicant respectfully submits that the Che et al. reference is not anticipatory with respect to amended claim 1. For a finding of anticipation under 35 U.S.C. §102(b), every element of the claimed invention must be found in the reference. It is argued that the Che et al. reference teaches a diethanolamine-derivatized polystyrene resin that has 8% cross-linking and which is outside of Applicant's claimed range. As such, Applicant respectfully submits that compositions of Che et al. do not fall within the instant claimed invention, and thus is not anticipatory with respect to claim 1 or any other claim in the presently pending claims, all of which include as a limitation that the solid support comprise a cross-linked polystyrene having about 1% to 2% cross-linking.

ii. The rejection under 35 USC. § 103(a)

Claims 2, 4-12 and 85 stand rejected under 35 USC. § 103(a) as allegedly being unpatentable over the Che et al. reference. In this regard, the Examiner has stated that Applicant discloses polymers which are identical to those disclosed in Che et al. except in claim 2, for the specific alkyl group pendant from the styrene entity, and for other claims, in the polymer substrate used. The Examiner has also stated that these various alkyl groups on styrene polymers are known in the prior art and has taken the position that the use of a homolog of the specific teaching of the reference would be prima facie obvious to one of skill in the art absent evidence of unexpected results commensurate in scope with the claims. The Examiner has also stated that Applicant's stipulation in their response of November 3, 2003 that the species mentioned in the election as to both the substrate polymers and the compound being produced further supports the position that the species are obvious one over the other, and that this is clearly true with reference to claims 4-12 wherein the polymer substrate is different and applicant has stipulated that these are merely obvious variants over the other. Applicant respectfully traverses this rejection for the reasons that are below.

Applicant submits that the claims as presently amended call for dihydroxyalkylaminobenzyl- or dihydroxyalkylaminoalkyl-conjugated solid supports, wherein the dihydroxyalkylamino moiety comprises the formula $\text{HO}(\text{CH}_2)_2\text{N}(\text{CH}_2)_2\text{OH}$, and wherein the solid support comprises a

cross-linked polystyrene having about 1% to 2% cross-linking. Che et al. provides diethanolaminomethyl-conjugated polystyrene resins for use in the production of polymer supported chelated titanate catalysts wherein the polystyrene has 8% cross-linking, and as such, is outside of the claimed range of the solid supports of the present invention. Moreover, it is the Applicant's respectful assertion that one of skill in the art would not have envisaged the presently claimed dihydroxyalkylaminobenzyl- or dihydroxyalkylaminoalkyl-conjugated solid supports, wherein the dihydroxyalkylamino moiety comprises the formula $\text{HO}(\text{CH}_2)_2\text{N}(\text{CH}_2)_2\text{OH}$, and wherein the solid support comprises a cross-linked polystyrene having about 1% to 2% cross-linking from the teachings of Che et al.

The Che et al. reference is directed to the synthesis and catalytic activity of polymer supported chelated titanates for use as catalysts. The Che et al. reference describes polymer supported inorganic chelated titanate catalysts which are prepared by the reaction of a carrier diethanolamine-derivatized polystyrene resin with ethylenedioxy dibutyl titanate. Page 2 of the English translation of the Che et al. reference provides that the polymer supported catalysts are prepared from PSCH_2Cl resin, wherein the resin has 8% cross-linking. Importantly, the Che et al. reference is designed to provide polymer-supported inorganic catalysts, and the working examples in the Che et al. reference disclose the use of diethanolamine-derivatized polystyrene resin that is 8% cross-linked as a polymer support for an inorganic chelated titanate catalyst. Nowhere does the Che et al. reference contemplate the preparation or use of Applicant's claimed solid supports having Applicant's solid supports having the claimed range of about 1-2% cross-linking for use in solid-phase immobilization and transformation. Applicant clearly teaches in the description as filed at page 27, paragraph 362 that higher degrees of cross-linking found in macroreticular resins (8%-20% of cross-linking) generally provide materials of much lower efficiency for use in solid-phase chemistries, and that higher degrees of cross-linking have been shown to be unsuitable for solid-phase immobilization and synthetic transformations of small boronic-acid containing organic compounds.

Moreover, Applicant submits that the presently claimed dihydroxyalkylaminobenzyl- or dihydroxyalkylaminoalkyl-conjugated solid supports, wherein the dihydroxyalkylamino moiety comprises the formula $\text{HO}(\text{CH}_2)_2\text{N}(\text{CH}_2)_2\text{OH}$, and wherein the solid support comprises a cross-

linked polystyrene having about 1% to 2% cross-linking show surprising results that could not have been predicted. Solid supports in the literature that can immobilize boronic acids have been shown to require harsh immobilization conditions relative to those for Applicant's present solid supports. For example, in the article entitled, "*Boronic Ester as a Linker System for Solid Phase Synthesis*", authored by B. Carboni et al. in *Tetrahedron Letters*, 1999, 40, 797-7983, the authors teach polymer-supported 1,3-diol resins for use in immobilizing boronic acids, and at page 7980, third paragraph, the authors teach that the best results for immobilizing boron to the resin is provided by heating the diol resin and $\text{RB}(\text{OH})_2$ in refluxing THF. Likewise, footnote 10 of the Carboni et al. reference teaches that for attachment of boronic acids to the resins, three equivalents of the boronic acid is added to the resin in THF and the suspension is stirred for 16 hours under reflux.

Likewise, an article by Hans Weidmann et al., ("*Borsaure-Ester von N-substituierten Aminoalkoholen*", *Annalen Der Chemie – Justus Liebig*, 619 (103), pp. 28-35, 1958) teaches that immobilization of boronic acids on various N-alkyldiethanolamine adducts in the solution phase requires the step of azeotroping off water.

In contrast, solid supports of Applicant's claimed invention are described as being capable of immobilizing boronic acids using straightforward stirring and obviate the need for exhaustive removal of water in the immobilization process. For example, page 31, paragraph 376 of Applicant's description as filed provides that diethanolaminomethylated polystyrene ("DEAM-PS") resin having 1% cross-linking with divinylbenzene as prepared in Example 1 at page 29, paragraph 372, could couple almost quantitatively to equimolar amounts of arylboronic acids in dry THF or other suitable solvents after minutes, and that the formation of a stable resin-bound boronic acid ester adduct was highly favoured. Importantly, Applicant describes that there is no need to remove the water produced in the immobilization/esterification process (two water molecules are formed during the immobilization of a boronic acid as is shown in Figure 13 of the Application as filed), unlike for other types of diols, whether via solid-phase or solution phase, that typically require azeotropic removal of water which is typically done using chemical additives (dehydrating agents) or special glassware and apparatus to co-distill the water. This property constitutes a significant advantage over such other types of diols.

Moreover, Example 5 found at page 5, paragraph 447 onwards of the application as filed, describes a time profile of boronic acid release with variable amounts of water. The profile of Figure 12 as described in Example 5 illustrates that hydrolysis of DEAM-PS supported *p*-tolylarylboronic acid required a large excess of water (greater than 32 equivalents) to provide practically quantitative hydrolysis of the boronic acid from the DEAM-PS solid support. This supports the surprising ability of the claimed solid supports to immobilize boronic acids.

Finally, it is noted that, for a determination of obviousness, as enunciated by the Supreme Court in *Graham v. John Deere*, 383 U.S. 1, 148 USPQ 459 (1966), the claimed invention must be considered as a whole, the references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination, the references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention, and reasonable expectation of success is the standard to which obviousness is determined. For the following reasons, Applicant submits that these criteria have not been met and a prima facie case of obviousness has not been established in this case based on the Che et al. reference.

First, the Examiner has failed to consider the Che et al. reference as a whole. The Che reference discloses polymer-supported chelated titanate compounds that are suitable for use as inorganic catalysts. All of the examples in the Che et al. reference relate to the use of the polymer-supported chelated titanates as inorganic catalysts. Moreover, the Che et al. reference fails to suggest the desirability of diethanolamine-derivatized polystyrene solid supports having about 1- 2% cross-linking of Applicant's instant invention, despite the long-felt need in the art for such solid-phase supports as is evidenced at pages 2 and 3 of the description as filed. Finally, the Che et al. reference fails to provide a sound basis for a reasonable expectation of success in providing diethanolamine-derivatized polystyrene solid supports having about 1- 2% cross-linking of Applicant's instant invention that afford immobilization of boronic acids via simple stirring and obviate the need for azeotroping of water formed during the immobilization process, as Che et al. is devoid of such a disclosure, suggestion or appreciation of such solid supports.

In view of the foregoing remarks, it is clear that there would have been no motivation based on Che et al. to arrive at the presently claimed solid supports. Absent any such motivation, it is clear that a prima facie case of obviousness against claims 1, 2 and 4 has not been made.

Finally, Applicant notes that in their November 3, 2003 reply to the Examiner's report of October 1, 2003 which requested restriction of the claims, Applicant elected Group I (claims 1-12) and new claim 85 for prosecution in this application with traverse. Moreover, in response to the election of species requirement, Applicant was required to elect a single species for initial examination on the merits if Groups I-IV were elected. In Applicant's November 3, 2003 reply, and further to Applicant's election of Group I, Applicant elected polystyrene as a specific polymer support only insofar as it is a requirement under the election of species requirement to facilitate initial examination, and in Applicant's view, the different species of Group I should have been examined in the present application. Applicant respectfully submits that arguments presented in their November 3, 2003 response in respect of the restriction requirement of October 1, 2003, relate solely to the Applicant's assertion that the species of the claims of Group I should have been examined in the present application, and do not constitute an admission with respect to the patentability of the species as claimed in Group I, one over the other. Applicant respectfully reminds the Examiner that under 37 C.F.R. § 1.141, more than one species of an invention may be specifically claimed in different claims of one application, so long as the application also includes an allowable generic claim embracing the distinct species. Applicant submits that the various species as claimed in Group I represented species of the broad genus claim of Group I.

Applicant has presently specified by way of the foregoing amendments that all of the currently pending claims include the limitation that the polymer solid support comprises a polystyrene, and further, that this polystyrene have about 1 to 2% cross-linking. Applicant previously elected polystyrene as a specific polymer support under the election of species requirement.

In view of the foregoing, Applicant respectfully submits that the presently amended claims are patentably distinct, and are patentable over the reference of Che et al.

Withdrawal of the obviousness rejection is accordingly respectfully requested.

iii. Claim Amendments and New claims

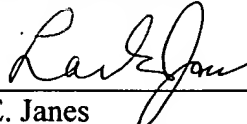
Claim 1 incorporates the limitation of former claim 3 and has been further amended to specify that the solid support comprises a cross-linked polystyrene resin having between about 1-2% cross-linking, support for which can be found at page 5, paragraph 263. Claim 2 has been amended to encompass embodiments where the dihydroxyalkylaminoalkyl group includes a diethanolaminomethyl group, support for which can be found at page 19, paragraph 334 as filed. Claim 4 has been amended to incorporate the limitation of former claim 5 to specify that the cross-linked polystyrene comprises a cross-linked poly(styrene-divinylbenzene) copolymer having about 1% to 2% cross-linking. New claim 86 has been added to specify that the solid support comprises a cross-linked poly(styrene-divinylbenzene) copolymer having about 1% cross-linking, support for which can be found at Example 1 at page 29 onwards of the description as filed. New claims 87-89 are directed to N,N-diethanolaminomethyl-conjugated solid supports, wherein the solid support comprises a cross-linked polystyrene resin having between about 1-2% cross-linking, support for which can be found at Example 1 at page 29 onwards of the description as filed.

No new matter is entered.

It is now believed that the present application is in condition for allowance and action to that end is respectfully solicited.

Respectfully submitted,

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Attachments: PTO/SB/21; PTO/SB/17; PTO/SB/22; PTO/SB/08b and references listed therein.